# This Page Is Inserted by IFW Operations and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

## IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

#### **Claims**

- 1. A method of inhibiting angiogenesis in a subject in need of such treatment comprising administering to the subject at least one antiangiogenic nucleic acid molecule in an amount effective to inhibit angiogenesis in the subject.
- 2. The method of claim 1, wherein the at least one antiangiogenic nucleic acid molecule comprises at least one sequence set forth as SEQ ID NOs: 1-1093.

5

COLYGGS TETROL

25

- 3. The method of claim 1, wherein two or more antiangiogenic nucleic acid molecules are administered.
- 4. The method of claim 1, further comprising administering to the subject at least one non-nucleic acid angiogenesis inhibitor molecule.
- 5. The method of claim 1, wherein the angiogenesis is associated with a condition selected from the group consisting of a solid tumor growth, a tumor metastasis, and a precancerous lesion.
- 6. The method of claim 1, wherein the nucleic acid is a CpG nucleic acid having an unmethylated CpG motif.
  - 7. The method of claim 1, wherein the nucleic acid is a T-rich nucleic acid.
  - 8. The method of claim 1, wherein the nucleic acid is a poly G nucleic acid.
  - 9. The method of claim 1, wherein the nucleic acid is isolated.
  - 10. The method of claim 1, wherein the nucleic acid does not encode a protein having antiangiogenesis activity.
  - 11. The method of claim 1, wherein the nucleic acid has a modified backbone.

- 12. The method of claim 11, wherein the modified backbone is a phosphate backbone modification.
- 13. The method of claim 11, wherein the modified backbone is a peptide modified oligonucleotide backbone.
  - 14. The method of claim 1, further comprising administering to the subject at least one anticancer agent.
  - 15. The method of claim 1, further comprising administering to the subject at least one antiarthritis agent.
  - 16. The method of claim 6, wherein the CpG nucleic acid comprises:

 $1/5' X_1 X_2 CGX_3 X_4 3'$ 

wherein C is unmethylated, and wherein X<sub>1</sub>X<sub>2</sub> and X<sub>3</sub>X<sub>4</sub> are nucleotides.

- 17. The method of claim 16, wherein the 5' X<sub>1</sub> X<sub>2</sub>CGX<sub>3</sub> X<sub>4</sub> 3' sequence is a non-palindromic sequence.
- 20 18. The method of claim/16, wherein the CpG nucleic acid has 8 to 100 nucleotides.

The method of claim 16, wherein X<sub>1</sub>X<sub>2</sub> are nucleotides selected from the group consisting of: GpT, GpG, GpA, ApA, ApT, ApG, CpT, CpA, CpG, TpA, TpT, and TpG; and X<sub>3</sub>X<sub>4</sub> are nucleotides selected from the group consisting of: TpT, CpT, ApT, TpG, ApG, CpG,

- 25 TpC, ApC, CpC, TpA, ApA, and CpA
  - 20. The method of claim 16, wherein  $X_1X_2$  are selected from the group consisting of GpA and GpT and  $X_3X_4$  are TpT.
- 30 21. The method of claim 16, wherein  $X_1X_2$  are both purines and  $X_3X_4$  are both pyrimidines.
  - 22. The method of claim 16, wherein  $X_2$  is a T and  $X_3$  is a pyrimidine.

- 3. The method of claim 16, wherein the CpG nucleic acid is 8 to 40 nucleotides in length.
- 24. The method of claim 16, wherein the CpG nucleic acid has a sequence selected from the group consisting of SEQ ID NOs: 1, 3, 4, 14-16, 18-24, 28, 29, 33-46, 49, 50, 52-56, 58, 64-67, 69, 71, 72, 76-87, 90, 91, 93, 94, 96, 98, 102-124, 126-128, 131-133, 136-141, 146-150, 152-153, 155-171, 173-178, 180-186, 188-198, 201, 203-214, 216-220, 223, 224, 227-240, 242-256, 258, 260-265, 270-273, 275, 277-281, 286-287, 292, 295-296, 300, 302, 305-307, 309-312, 314-317, 320-327, 329, 335, 337-341, 343-352, 354, 357, 361-365, 367-369, 373-376, 378-385, 388-392, 394, 395, 399, 401-404, 406-426, 429-433, 434-437, 439, 441-443, 445, 447, 448, 450, 453-456, 460-464, 466-469, 472-475, 477, 478, 480, 483-485, 488, 489, 492, 493, 495-502, 504-505, 507-509, 511, 513-529, 532-541, 543-555, 564-566, 568-576, 578, 580, 599, 601-605, 607-611, 613-615, 617, 619-622, 625-646, 648-650, 653-664, 666-697, 699-706, 708, 709, 711-716, 718-732, 736, 737, 739-744, 746, 747, 749-761, 763, 766-767, 769, 772-779, 781-783, 785-786, 7900792, 798-799, 804-808, 810, 815, 817, 818, 820-832, 835-846, 849-850, 855-859, 862, 865, 872, 874-877, 879-881, 883-885, 888-904, and 909-913.
  - 25. The method of claim 7, wherein the T-rich nucleic acid is a poly T nucleic acid comprising

5' TTTT 3'.

- 26. The method of claim 25, wherein the poly T nucleic acid comprises by X<sub>1</sub> X<sub>2</sub>TTTTX<sub>3</sub> X<sub>4</sub> 3'
- wherein X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub> and X<sub>4</sub> are nucleotides.
  - 27. The method of claim 25; wherein the T rich nucleic acid comprises a plurality of poly T nucleic acid motifs.
- 30 28. The method of claim 26, wherein  $X_1X_2$  is TT.
  - 29. The method of claim 26, wherein  $X_3X_4$  is T.

15

- The method of claim 26, wherein X<sub>1</sub>X<sub>2</sub> is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC.
- The method of claim 26, wherein X<sub>3</sub>X<sub>4</sub> is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, CG, GT, GG, GA, and GC.
  - 32. The method of claim 25, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 25% T.
  - 33. The method of claim 7, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 25% T.
    - 34. The method of claim 33, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 30% T.
    - 35. The method of claim 33/wherein the T rich nucleic acid comprises a nucleotide composition of greater than 50% T.
- 36. The method of claim 33, wherein the Trich nucleic acid comprises a nucleotide composition of greater than 60% T
  - 37. The method of claim 33, wherein the T rich nucleic acid comprises a nucleotide composition of greater than 80% T.
- 25 38. The method of claim 7, wherein the T rich nucleic acid comprises at least 20 nucleotides.
  - 39. The method of claim 7, wherein the T rich nucleic acid comprises at least 24 nucleotides.
  - 40. The method of claim 8, wherein the poly G nucleic acid comprises:

5' X<sub>1</sub>X<sub>2</sub>GGGX<sub>3</sub>X<sub>4</sub>3'

wherein  $X_1$ ,  $X_2$ ,  $X_3$ , and  $X_4$  are nucleotides.

30

5

- The method of claim 40, wherein at least one of  $X_3$  and  $X_4$  are a G.
- 42. The method of claim 40, wherein both of  $X_3$  and  $X_4$  are a G.
- 43. The method of claim 8, wherein the poly G nucleic acid comprises the following formula:

#### 5' GGGNGGG3'

wherein N represents between 0 and 20 nucleotides.

44. The method of claim 8, wherein the poly G nucleic acid comprises the following formula:

### 、p' &GGNGGGNGGG 3'

wherein N represents between 0 and 20 nucleotides.

- 45. The method of claim 8, wherein the poly G nucleic acid is free of unmethylated CG dinucleotides
- 46. The method of claim 45, wherein the poly G nucleic acid is selected from the group consisting of SEQ ID NOs: 5, 6, 73, 215, 267-269, 276, 282, 288, 297-299, 355, 359, 386, 387, 444, 476, 531, 557-559, 733, 768, 795, 796, 914-925, 928-931, 933-936, and 938.
  - 47. The method of claim 8, wherein the poly G nucleic acid includes at least one unmethylated CG dinucleotide.
  - 48. The method of claim 47, wherein the poly G nucleic acid is selected from the group consisting of SEQ ID NOs: 67, 80-82, 141, 147, 148, 173, 178, 183, 185, 214, 224, 264, 265, 315, 329, 434, 435, 475, 519, 521-524, 526, 527, 535, 554, 565, 609, 628, 660, 661, 662, 725, 767, 825, 856, 857, 876, 892, 909, 926, 927, 932, and 937.
  - 49. The method of claim 1, wherein the nucleic acid is a synthetic nucleic acid.
  - 50. The method of claim 9, wherein the nucleic acid is administered on a routine schedule.

- The method of claim 1, wherein the angiogenesis is associated with a condition selected from the group consisting of rheumatoid arthritis, psoriasis, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, wound granulation, intestinal adhesions, atherosclerosis, scleroderma, and hypertrophic scars.
- 52. The method of claim 1, wherein the nucleis acid is not an antisense molecule.
- 53. A pharmaceutical composition comprising an amount of at least one antiangiogenic nucleic acid molecule effective to inhibit angiogenesis and a pharmaceutically acceptable carrier.
- 34. The pharmaceutical composition of claim 53, wherein the at least one antiangiogenic nucleic acid molecule comprises at least one sequence set forth as SEQ ID NOs: 1-1093.
- 55. The pharmaceutical composition of claim 53, wherein two or more antiangiogenic nucleic acid molecules are administered.
- 56. The pharmaceutical composition of claim 53, further comprising at least one non-nucleic acid angiogenesis inhibitor molecule.
- 57. The pharmaceutical composition of claim 53, wherein the antiangiogenic nucleic acid molecule has a modified backbone.
- 58. The pharmaceutical composition of claim 57, wherein the modified backbone is a phosphate modified backbone.
- 30 59. The pharmaceutical composition of claim 58, wherein the phosphate modified backbone is a phosphorothioate modified backbone.
  - 60. The pharmaceutical composition of claim 53, further comprising an anticancer agent.

25

30

- The pharmaceutical composition of claim 53, wherein the nucleic acid is a CpG nucleic acid.
- 5 62. The pharmaceutical composition of claim 53, wherein the nucleic acid is a T-rich nucleic acid.
  - 63. The pharmaceutical composition of claim 53, wherein the nucleic acid is a poly G nucleic acid.
  - 64. The pharmaceutical composition of claim 53, wherein the nucleic acid is isolated.
  - 65. The pharmaceutical composition of claim 53, wherein the nucleic acid is not an antisense molecule.
  - 66. Akit comprising

a first container housing at least one antiangiogenic nucleic acid molecule, and instructions for administering the antiangiogenic nucleic acid to a subject having a condition characterized by unwanted angiogenesis.

- 67. The kit of claim 66, wherein the antiangiogenic nucleic acid has a modified backbone.
- 68. The kit of claim 67, wherein the modified backbone is a phosphate modified backbone.
- 69. The kit of claim 67, wherein the phosphate modified backbone is a phosphorothioate modified backbone.
- 70. The kit of claim 65, further comprising a second container housing at least one non-nucleic acid antiangiogenic agent.
- 71. The kit of claim 65, further comprising a second container housing at least one anticancer agent.

- 72. The kit of claim 69, further comprising a third container housing at least one anticancer agent.
- 5 73. The kit of claim 65, wherein the nucleic acid is not an antisense molecule.
  - 74. The kit of claim 65, wherein the instructions relate to administering the antiangiogenic nucleic acid to a subject having a condition selected from the group consisting of rheumatoid arthritis, psoriasis, diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular glaucoma, retrolental fibroplasia, rubeosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, wound granulation, intestinal adhesions, atherosclerosis, scleroderma, and hypertrophic scars.